

## PHARMACOLOGY

## Goitrogenic Activity of Onion Volatiles

GOITRE is known to be prevalent in the Lebanon, mainly in the high mountain valleys<sup>1-5</sup>. In an investigation of the population of an endemic area in the Lebanon, Cowan *et al.*<sup>6</sup> found that iodine deficiency was the primary cause of the endemic goitre. This deficiency could be intensified by the consumption of goitrogenic foods which cause either an increased iodine excretion or an inhibition of the biosynthesis of the thyroid hormone, thyroxine.

Two sulphur-containing substances, thiourea and thiouracil, have been found to inhibit the iodization process of thyroxine<sup>7</sup>. In addition, thiocyanate and thio-oxazolidone-forming substances, in plants mainly of the Cruciferae family, have been shown to be goitrogenic<sup>8-11</sup>. However, there have been no reports on the possible goitrogenicity of onions, although sulphur compounds are known to be the principal components of their oils<sup>12,13</sup>.

Onions are grown extensively in the Lebanon and are consumed in great amounts by the Lebanese people; thus an investigation of the possible goitrogenic activity of this plant is important. Saghir *et al.*<sup>14</sup> found that propyl disulphide is the main volatile constituent of certain food onions (common onion, *Allium cepa*; leek, *A. ampeloprasum*; Japanese bunching onion, *A. fistulosum*; and chive, *A. schoenoprasum*). This compound was therefore selected to be tested for its goitrogenic effect. Preliminary experiments indicated that 5  $\mu$ l. and 10  $\mu$ l. doses of the chemical slightly inhibited thyroid function in rats. The present work was initiated to investigate the effects of high levels of this sulphide.

Synthetic *n*-propyl disulphide (PDS) was obtained in pure form from Eastman Organic Chemicals; previous work had shown this compound to be identical to that found in onions<sup>12,13</sup>. For the assessment of goitrogenicity, the "acute" test described by Langer and Stole<sup>15</sup> was used. The experimental animals were young female albino rats of the Sprague-Dawley strain, weighing about 150 g. Because the test was based on short-period (3 h) values for radioiodine uptake, iodine-deficient animals were used so that the control values would be relatively high. The rats were rendered deficient in iodine by maintaining them on a low iodine diet for 6 weeks. This diet was complete except for iodine, and the animals grew normally during the period of iodine depletion.

Five animals were assigned to each of seven test groups, according to a randomized block design, based on body weight. "Normal" uptake values were obtained from a control group which received only corn oil (since the test material was an oil). To check the validity of the test by demonstrating definite inhibition of thyroid function, two groups of rats were treated with two levels of a known goitrogen, propyl thiouracil (PTU).

The animals were fasted overnight before the experiment; the appropriate amounts of corn oil, PTU or PDS (Table 1) were then administered by stomach tube. 1 h later, each rat received, by intraperitoneal injection, 1  $\mu$ c. of carrier-free sodium iodide labelled with iodine-131 in 0.5 ml. of 0.9 per cent saline solution. Exactly 3 h later, the animals were killed with chloroform and the thyroids were removed and weighed. Each gland was digested overnight at 50° C in a tube containing 2 ml. of alcoholic potassium hydroxide (potassium hydroxide, 5 g; water, 50 ml.; ethanol, 100 ml.). Total radioactivity was measured in each tube using a well-type crystal scintillation counter (Baird-Atomic). Percentage uptake was calculated by comparing the counts per mg thyroid tissue with those obtained from a standard dose counted at the same time as the thyroid digests.

The results are shown in Table 1. It is clear that at all levels used, *n*-propyl disulphide inhibited thyroid function

Table 1. EFFECT OF VARIOUS LEVELS OF *n*-PROPYL DISULPHIDE AND PROPYL THIOURACIL ON THE UPTAKE OF IODINE-131 IN RATS

Treatment	Dose	Average percentage uptake of iodine-131 per mg tissue*
Corn oil	100 $\mu$ l.	1.176
PTU	1 mg	0.060
PTU	2 mg	0.080
PDS	60 $\mu$ l.	0.070
PDS	120 $\mu$ l.	0.080
PDS	180 $\mu$ l.	0.087
PDS	240 $\mu$ l.	0.103
LSD†		0.053

\* Average of five values.

† Least significant difference (5 per cent level).

significantly as is shown by the low values for uptake of iodine-131 in the treated animals. These low values were similar to those obtained by treatment with PTU. These observations point to the possibility that the consumption of food onions high in PDS may contribute to the incidence of goitre in countries such as the Lebanon where iodine intake is low. Further work is planned to investigate the possible goitrogenic effects of other sulphide radicals known to be constituents of other *Allium* species.

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## 6-Hydroxyskatole Glucuronide, a Skatole Metabolite

THE metabolism of 6-hydroxylated indoles is of interest in view of their possible psychotoxicity as reported by Szara<sup>1</sup> and the finding, originally by Leyton<sup>2</sup>, that 6-hydroxyskatole sulphate is excreted in larger amounts by schizophrenic patients.

Hydroxylation and subsequent conjugation with either sulphate or glucuronic acid has been shown to be a pathway for the detoxification of a number of indoles. Skatole has been shown to undergo hydroxylation primarily in the 6 position and subsequent conjugation with sulphate<sup>3</sup>. Melatonin, another 6-hydroxylated indole, is excreted both as the sulphate and the glucuronide<sup>4</sup>. This report presents evidence that 6-hydroxyskatole is also excreted as the glucuronide.

6-Hydroxyskatole was prepared according to the method of Heacock<sup>5</sup> from 6-benzyloxygramine by catalytic hydrogenation. The compound was administered to 150-g Sprague-Dawley male rats in doses of 0.1, 1, 10, 25 and 50 mg/kg. Urine was collected at 2-h intervals